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MEMORANDUM

DATE: December 16, 2004

SUBJECT: Risk Assessment for Methyl Eugenol (Methyleugenol)

DP Barcode: D302237 PC Code: 203900

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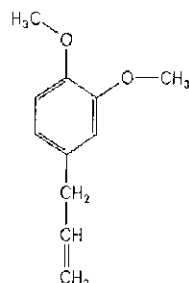
Executive Summary: This memo is the Tolerance Reassessment Eligibility Decision (TRED) assessment for methyl eugenol. Only potential dietary risk is assessed in this memo.

Methyl eugenol is an insect attractant used in insect traps for control of fruit flies in orchards. Traps containing methyl eugenol are placed near fruit trees, but methyl eugenol is not used on the fruit or trees. Since methyl eugenol is a volatile chemical that rapidly dissipates in air, there is little possibility of contamination of fruit from nearby traps. This was confirmed by a monitoring study by the California Department of Food and Agriculture which did not detect methyl eugenol in fruit collected near sites of methyl eugenol use. Methyl eugenol is a natural constituent of many foods and is considered GRAS (Generally Recognized As Safe) by the FDA. There is an exemption for the requirement for a tolerance for methyl eugenol under CFR 180.1067.

Although there is hazard found in rodent toxicity studies, the potential for human dietary exposure to this chemical is below a level of quantitation. Therefore, there are no risk concerns for dietary exposure to methyl eugenol in food or water.

Chemical characteristics: Methyl eugenol is a colorless liquid with the odor of cloves. Water solubility is < 0.1 g/100mL (19°C). Vapor pressure is 0.01 mm Hg at 20°C. The CAS # is 93-15-2.

Structure:



Non-pesticidal sources of methyl eugenol exposure: Methyl eugenol is a natural ingredient in a number of plants and essential oils including cloves, basil, nutmeg, mace, anise, laurel leaves, and orange peels, among others. Clove oil is about 15% methyl eugenol, and other oils also contain high concentrations of methyl eugenol. Clove and its derivatives are affirmed as GRAS by FDA as flavoring agents under 21 CFR 172.515.

The National Institute of Environmental Health Sciences monitored the serum of adults for methyl eugenol. The median concentration was approximately 16 pg/g of serum and may indicate a daily consumption of approximately 6 ug methyl eugenol daily. The source of methyl eugenol exposure was attributed to the presence of methyl eugenol in many foods, both as a natural ingredient and as an approved food additive.

Use as an insect attractant: In previous experimental use permits by the U.S. Department of Agriculture, methyl eugenol was used as a bait in traps at the rate of 7.98 gram per trap and 1.5 traps per acre, which is equivalent to 12 grams per acre, or 0.026 lb ai/acre. This is an order of magnitude lower than the application rates for typical agricultural situations.

Hazard: Information about the toxicology of methyl eugenol came from open literature sources because the toxicology 1-liners only listed several acute studies. The OPP bibliography also listed a subchronic study, however the study report was illegible. Methyl eugenol was evaluated at the 23rd meeting of Joint WHO/SAO Expert Committee on Food Additives. No toxicology monograph was prepared at that time because of a lack of toxicity studies. Since then, the National Toxicology Program has sponsored several studies with methyl eugenol. Methyl eugenol caused a variety of neoplasms in rats and mice: liver neoplasms (hepatadenoma/carcinoma, hepatocholangioma/carcinoma, hepatoblastoma, kidney (adenoma/carcinoma), mammary fibroadenoma, subcutaneous fibroma/sarcoma, malignant mesothelioma, and neuroendocrine stomach lesions. Results of mutagenicity studies indicated that methyl eugenol caused unscheduled DNA synthesis and methyl eugenol metabolites formed DNA adducts.

Dietary exposure: The California Department of Food and Agriculture conducted monitoring of apricots, apples, and oranges near locations where methyl eugenol was used in fruit fly traps. A total of 56 samples were collected from an area 31 cm to 61 cm from the trap at time periods of 4 hours and 24 hours after the traps were re-baited. Methyl eugenol was not detected in apricot and apples. Positive results in oranges are attributed to the fact that methyl eugenol is a natural constituent of orange rinds and was found in control samples at concentrations ranging from 29 to 289 ppb, with an average of 170 ppb. The LOD using GC was 28 ppb and confirmation was by GC/MS.

Risk characterization: People are exposed to non-pesticidal methyl eugenol from a variety of dietary sources because of methyl eugenol's presence as a natural constituent of many foods. The insect attractant, methyl eugenol, is not applied to any food crops but is only used near orchards. Because of its volatility and because of its use patterns, it is considered unlikely for methyl eugenol to contaminate food or drinking water. This was confirmed by the above-mentioned California Department of Food and Agriculture monitoring study which did not detect methyl eugenol from pesticide sources in fruit collected near sites of methyl eugenol use. Therefore, there are no risk concerns for methyl eugenol used as an insect attractant in insect traps.

Bibliography: Barr, DB; *et al* (2000). Levels of methyleugenol in a subset of adults in the general U.S. population. *Env. Health Perspectives*, 2000. 108 (4): 323-328.

Carr, NV; Gallavan, R; Tran, D (1990). Monitoring of methyl eugenol and DDVP in fruit near fruit fly traps during a pest trapping program. Department of Food and Agriculture, State of California.

Johnson, JD; *et al.* (2000). Two-year toxicity and carcinogenicity study of methyleugenol in F344/N rats and B6C3F1 mice. Battelle Columbus Laboratories and National Institute of Environmental Health Sciences. *J. Agr. Food Chem.* 2000, 48: 3620-3632.

Smith, RL; *et al* (2001). Safety assessment of allylalkoxybenzene derivatives used as flavoring substances - methyl eugenol and estragole. *Food Chem. Tox.* 40: 851-870.



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